Remarks

Rejection Under 35 U.S.C. § 103

Claims 16 and 18 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,188,837 to Domb ("Domb"). Claims 16 and 17 were rejected under 35 U.S.C. 103(a) as being unpatentable over European Patent No. EP 0 257 915 to Boyes *et al.* ("Boyes"). Claims 16, 19, and 20 were rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,063,910 to Debenedetti *et al.* ("Debenedetti"). Claims 16 and 21 were rejected under 35 U.S.C. 103(a) as being unpatentable over Japanese Patent No. JP 363020301 to Sugaya *et al.* ("Sugaya"). Claim 22 was rejected under 35 U.S.C. 103(a) as being unpatentable over European Patent No. EP 0 257 915 in view of U.S. Patent No. 4,866,051 to Hunt *et al.* ("Hunt"). Applicants respectfully traverse these rejections.

The Legal Standard

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not in the applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

To establish *prima facie* obviousness of a claim, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). Additionally, if an independent claim is nonobvious under 35 U.S.C. § 103, then any claim depending therefrom is also nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Analysis

U.S. Patent No. 5,188,837 to Domb ("Domb")

Domb describes a microsuspension system containing lipospheres, which are solid, water-insoluble microparticles that have a layer of phospholipid embedded on their surface (abstract). The product is a uniform fine dispersion of microparticles in an *aqueous medium* (col. 6, lines 16-20, emphasis added). Domb does not disclose or suggest **dry** microparticles, as required by claims 16 and 18. Further, Domb does not disclose or suggest microparticles that release a drug at a pH of greater than 6.0. Therefore, claims 16 and 18 are not obvious over Domb.

European Patent No. 0 257 915 to Boyes et al. ("Boyes")

Boyes describes a pharmaceutical formulation including polymeric microcapsules and a lipid-soluble surfactant that is mixed with the microcapsules or is incorporated within or coats the wall material of the microcapsules (abstract). The formulations can be in the form of an aerosol or dry powder for inhalation, or an aqueous-oil emulsion for oral administration

(abstract). Boyes discloses that "by an appropriate selection of polymeric materials, a formulation can be made such that the resulting microcapsules remain intact until all of the drug is released" (page 3, lines 48-50). Boyes does not disclose or suggest that the release of the active agent from the microcapsules can be pH-mediated. In contrast, the claimed compositions are designed to release the incorporated drug at a pH of greater than 6.0 (*see e.g.* Claim 16). Accordingly, the claims 16 and 18 are not obvious over Boyes.

U.S. Patent No. 6,063,910 to Debenedetti et al. ("Debenedetti")

Debenedetti describes a method for the formation of microparticles, particularly protein microparticles, from a solution by antisolvent recrystallization using a supercritical fluid (col. 2, lines 23-26). The protein microparticles can be used to prepare devices with controlled rates of release by uniformly dispersing the protein microparticles within a polymer matrix (col. 3, lines 23-29). Debenedetti discloses that the polymer particles should be small (i.e. < 50 μm) so that they can be injected (col. 3, lines 29-30).

Debenedetti discloses drug delivery via *injection* and does not disclose or suggest microparticles comprising a drug to be delivered by *inhalation*. Debenedetti does not disclose or suggest that the release of the active agent from the microparticles can be pH-mediated, let alone suggest microparticles that are designed to release drug at a pH of greater than 6.0. Therefore, the claims 16, 19 and 20 are not obvious over Debenedetti.

Japanese Patent Application No. JP 63020301 to Sugaya et al. ("Sugaya")

Sugaya describes microparticles prepared from chitosan with an average diameter of less than 10 μm. The microparticles are prepared by dissolving chitosan in a 0.1% to 10% by weight aqueous solution of an acid, such as acetic acid or hydrochloric acid, to obtain an acidic aqueous solution of chitosan of a concentration of 0.05% to 20% by weight (abstract). The solution is spray-dried without a coagulant, a suspending agent, or the like (abstract). The microparticles can be used as a carrier material in the medical field (abstract).

Sugaya does not disclose or suggest including in the microparticles a drug to be delivered by inhalation. Further, Sugaya does not disclose or suggest that the release of a drug from the microparticles can be pH-mediated, let alone specify that the microparticles are designed to release a drug at a pH greater than 6.0. Therefore, claims 16 and 21 are not obvious over Sugaya.

European Patent No. EP 0 257 915 in view of U.S. Patent No. 4,866,051 to Hunt et al. ("Hunt")

Hunt describes pharmaceutical compositions containing beclomethasone in the form of its micronized monohydrate (abstract). The compositions may be in the form of powder inhalation cartridges especially suitable for the treatment and/or prophylaxis of asthma (abstract). Hunt does not disclose or suggest that the release of the active agent from the microcapsules can be pH-mediated, let alone suggest that the microcapsules release drug at a pH of greater than 6.0, as required by claim 22.

The Combination of Boyes and Hunt

As discussed above, Boyes does not disclose or suggest that the release of a drug from the microcapsules can be pH-mediated, let alone specify that release occurs at a pH of greater than 6.0. Similarly, Hunt does not disclose or suggest that the release of the active agent from the microcapsules can be pH-mediated, let alone suggest that release occurs at a pH of greater than 6.0, as required by claim 22. Therefore, even if one of ordinary skill in the art combined Hunt with Boyes, claim 22 would not be obvious.

Double Patenting Rejections

Claims 23-36 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,427,771 to Steiner *et al.* Claims 23, 26-28, 31-33, and 36 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4-7, and 10-12 of U.S. Patent No. 6,071,497 to Steiner *et al.* In response, and solely to facilitate prosecution, Applicants submits a terminal disclaimer to overcome the double patenting rejections.

Amendment to claim 35

Claim 35 has been amended to correct an obvious grammatical error by inserting "wherein" before "X is fumaryl".

Allowance of claims 16-36, as amended, is respectfully solicited.

Respectfully submitted,

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